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In re Application of :  
SCHLINGENSIEPEN et al :  
Serial No.: 09/701,583 :Decision on Petition  
Filed : February 5, 2001 :  
Attorney Docket No.: P66141US0 :

This letter is in response to the Petition under 37 C.F.R. 1.144 filed on March 13, 2007 requesting reconsideration of the restriction requirement.

**BACKGROUND**

A review of the file shows that this is the national stage filing of PCT/EP99/04013 under 35 USC 371 and is eligible for PCT unity of invention rules.

On October 2, 2002, the examiner mailed a requirement to comply with the sequence rules.

On February 5, 2004, the examiner mailed a restriction requirement in which the original claims 1-13 were divided into 6 groups. The examiner further required applicants to select a single substance from Claim 1, a single stimulator from Claim 8 and a single nucleotide sequence from Claim 10.

On May 5, 2004, Applicants elected Group I (Claims 1-5, 7-8, 11-13), a tumor cell extract as the single stimulator; and SEQ ID No 7 as the oligonucleotide sequence with traverse.

On July 14, 2004 the examiner considered the traversal, made the restriction requirement FINAL. The examiner rejoined Group I and Groups V and VI (Claims 9-10) but maintained the restriction between Groups I, II, III and IV. The examiner mailed to applicants a non-final Office action, in which Group I (Claims 1-5, 7-13) drawn to SEQ ID NO 7 were searched and examined on the merits. The claims were rejected under 112, 2<sup>nd</sup> paragraph; 112, 1<sup>st</sup> paragraph for lack of enablement; and under 102(b) and 102(e). The examiner indicated that SEQ ID NO: 7 was free of the prior art searched.

On January 14, 2005, applicants filed a response to the Office action. The claims were amended to created Markush groupings in Claims 5 and 10, for example, rather than relying on Figures.

On April 4, 2005, the examiner mailed a subsequent non-final Office action.

On October 4, 2005, the applicants filed a response addressing the Office action and amending the independent claim to require one of SEQ ID NO:s 1-213.

On January 4, 2006, the examiner mailed a subsequent requirement for restriction. The requirement requested that applicant elect two additional nucleotide sequences in addition to the elected SEQ ID NO: 7 from claims 1 and 10.

On January 31, 2006, the applicant responded and elected SEQ ID NO: 9 and SEQ ID NO: 14 as the additional two sequences requested by the examiner. The response traversed the restriction stating that the SEQ ID NO: 1-32 are not independent and distinct from one another as they correspond to a single gene. It is noted that the claims pending at that time were directed to SEQ ID Nos 1-213 and there was no claim limited to SEQ ID Nos 1-32.

On April 21, 2006, the examiner mailed a non-final Office action in which Claims 1-2, 7-11 were rejected.

On September 21, 2006, applicants filed a response to the Office action. The response, on page 10, requests reconsideration of the final restriction/election requirement in view of MPEP 803.04.

On December 6, 2006, the examiner made a FINAL rejection of Claims 1-2, 7-11. The examiner acknowledged and considered the traversal.

On March 13, 2007, applicants filed this petition to request that the Office reconsider the restriction requirement(s).

## **DISCUSSION**

The petition and extensive file history have been carefully considered. Because this application has been filed under 35 USC 371, it is entitled to PCT unity of invention rules, however the restriction requirement was incorrectly set forth under US restriction requirement rules. Neither the examiner nor applicants have corrected or addressed this error. In this decision, PCT unity of invention rules will be applied to the currently pending claims.

### **I. Determining Unity of Invention**

The petition requests rejoinder of SEQ ID Nos 1-32 and 58-67 because they are all antisense oligonucleotides corresponding to a single gene encoding TGF-beta. This argument is not persuasive for the following reasons.

(1) The claims are not commensurate in scope with this argument. The Markush claims 1, 10 and the claims depending therefrom currently pending in this application are directed to sequences in addition to SEQ ID Nos 1-32 and 58-67. PCT Markush practice requires that all the alternatives of a Markush claim to share a single inventive concept. SEQ ID Nos 33-66 and 68-213 are not antisense oligonucleotides corresponding to the TGF-beta 2 gene. Specifically, SEQ ID NO: 33-54, 73-106 are drawn to TGF-B1; SEQ ID NO: 107-118 are drawn to TGF-B3; SEQ ID NO: 119-154 are drawn to VEGF, for example (see Figure 1). Moreover, Claim 6 is drawn to an antibody, it is not directed to an antisense oligonucleotide.

(2) In order for a Markush claim to have unity of invention, PCT Markush practice requires that the alternatives share a common structural feature and a common property or activity. The oligonucleotides of SEQ ID NO: 1-5, for example, do not share a common structure with each other. SEQ ID NO: 1-5 from Figure 1 has been reproduced below and do not appear to share any common structure. While they all bind to TGF-B2, they bind to different portions of TGF-B2 and they do not share a common structure present in every other SEQ ID NO:.

1.	TGF- $\beta$ 2-1	C ACA CAG TAG TGC A
2.	TGF- $\beta$ 2-2	GC ACA CAG TAG TGC
3.	TGF- $\beta$ 2-3	GC TTG CTC AGG ATC TGC
4.	TGF- $\beta$ 2-4	TAC TCT TCG TCG CT
5.	TGF- $\beta$ 2-5	C TTG GCG TAG TAC T

Moreover, the claims encompass oligonucleotides of SEQ ID NO: 33-37, for example, which do not share the common property of binding to TGF-B2 and do not share a common structure. SEQ ID NO: 33-37 are reproduced below and do not appear to share any common structure with each of the other SEQ ID NO:s.

33.	TGF- $\beta$ 1-1	CGA TAG TCT TGC AG
34.	TGF- $\beta$ 1-2	GTC GAT AGT CTT GC
35.	TGF- $\beta$ 1-3	CTT GGA CAG GAT CT
36.	TGF- $\beta$ 1-4	CCA GGA ATT GTT GC
37.	TGF- $\beta$ 1-5	CCT CAA TTT CCC CT

Finally Claim 6 is drawn to an antibody. DNA is composed of nucleotides linked in phosphodiester bonds and arranged in space as a double helix. The DNA can function not only for the expression of the protein but also as a probe in a nucleic acid hybridization assay and in a nucleic acid amplification assay, for example. In contrast, the antibody of Claim 6 is composed of amino acids linked in peptide bonds and arranged spatially in a very specific tertiary structure that allows that antibody to specifically bind to particular regions, i.e. epitopes, of the encoded polypeptide. The antibody can function for the detection and purification of the polypeptide to which it binds. The antibody and the nucleic acid oligonucleotides do not share a common structure or a common function.

(3) Moreover, even if the TGF-B2 sequences did share a common structure and a common property (which they do not), SEQ ID NO: 1-32, 58-67 lack a special technical feature which makes a contribution over the prior art.

The response asserts that each of the sequences share the same function. The response asserts that all these oligonucleotides inhibit TGF beta expression. It appears that applicants are arguing that the shared property, inhibiting TGF-B2 expression, makes a contribution over the prior art. This argument is not persuasive. The prior art Schlingensiepen (WO 94/25588, November 10, 1994) teaches antisense oligonucleotides for transforming growth factor -B (TGF-B). Schlingensiepen provides nearly 140 antisense molecules which would inhibit TGF-B expression. The instant SEQ ID NO: 1-32, 58-67 thus do not share a special technical feature that makes a contribution over the prior art.

(4) Restriction within a claim of a 371 application is permitted by 37 CFR 1.475(e).

37 CFR 1.475(e) states that:

- (e) **The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.**

Thus, as provided by 37 CFR 1.475(e), the examiner is not obligated to search and examine SEQ ID Nos 1-6, 8, 10-13, 15-213 just because they are listed in the alternative of a single claim.

## II. Consideration of MPEP 803.04 in view of the March 27, 2007 OG Notice.

The petition asserts that the examination is inconsistent with Manual of Patent Examining Procedure (MPEP) 803.04. The petition states that the restriction improperly limited election to only one nucleotide sequence, instead of 10 nucleotide sequences and limited examination to only the one elected sequence together with only two patentably indistinct sequences instead of all antisense oligonucleotides corresponding to a single gene encoding a single protein. The petition cites MPEP 803.04 directed to the 1996 OG Notice, which granted a partial waiver for independent and distinct inventions. This argument has been reviewed but is not convincing.

An OG Notice published March 27, 2007 rescinded the 1996 OG Notice that provided for a partial waiver of the requirements for restriction practice by permitting examination of a reasonable number, up to ten, independent and distinct polynucleotide molecules in a single 35 USC 111(a) or 35 USC 371 application. The Notice indicated that the standard of independence and distinctness would be applied to polynucleotide claims filed in an application under 35 USC 111(a).

Additionally, the March 27, 2007 OG Notice specifically spoke to the issue of burden of searching more than one independent and distinct invention.

The petition asserts that SEQ ID NO: 1-32 and 58-67 must be examined together because nucleotide sequence encoding the same protein are not considered to be independent and distinct. This argument has been reviewed but is not persuasive. It is noted that the claimed SEQ ID NO:s do not encode a protein because they are all short sequences corresponding to the non-coding strand. For example, SEQ ID NO: 1 is 14 nucleotides in length. This length is too short to encode a protein.

Finally, the 1996 OG Notice was permissive in nature and not mandatory. The 1996 OG Notice permitted examination of a reasonable number, within the range of up to ten, of polynucleotide inventions. One polynucleotide molecule is within the permitted range.

### III. Consideration of Obvious Variants

The petition argues that limited examination to only the elected sequences (SEQ ID NO: 7) together with only 2 patentably indistinct sequences (SEQ ID NO: 9 and 14), instead of together with all of SEQ ID NO: 1-32 and 58-67, as antisense oligonucleotides corresponding to a single gene encoding a single protein is improper (page 7 of the petition). It is not entirely clear whether the petition is asserting that SEQ ID NO: 1-32 and 58-67 are patentably indistinct from one another. If applicants would like to state with clarity on the record that SEQ ID NO: 1-32 and 58-67 are patentably indistinct one from another, because they would be obvious variants, with each other, the Office would be willing to consider each of the oligonucleotides within the same group.

The MPEP sets forth a means for applicant to assert on the record that SEQ ID NO: 1-32 and 58-67 are obvious variants over one another and as such are not independent or distinct. Specifically, the MPEP provides that "Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention." The applicants do not appear to have availed themselves of this opportunity to place such evidence or statements on the record.

Thus, for the reasons provided above, the requirement to restrict this application to the elected sequences, SEQ ID NO: 7, 9 and 14 has been affirmed.

### DECISION

The petition is **DENIED** for the reasons set forth above.

Claim 6 and SEQ ID Nos 1-6, 8, 10-13, 15-213 remain withdrawn from consideration. Claims 1, 2, 7-11 are under examination to the extent that they read upon elected SEQ ID Nos 7, 9 and 14.

Any request for reconsideration must be filed within two (2) months of the mailing date of this decision.

Applicants remain under obligation to timely respond to the Final Office action mailed 6 December 2006 with the time period set within the Final Office action mailed 6 December 2006.

Should there be any questions about this decision, please contact Special Program Examiner Julie Burke, by letter addressed to Director, Technology Center 1600, at the address listed above, or by telephone at 571-272-1600 or by facsimile sent to the general Office facsimile number, 571-273-8300.

A handwritten signature in black ink, appearing to read "Chris Low", written in a cursive style.

Chris Low  
Director, Technology Center 1600  
jb/jg